REMARKS

Claims 2, 3, 5, 10-12, 17-19, 25 and 27-34 are currently under consideration. Claims 11, 17, 18, 19, 27, 30 and 32 are amended to address points raised in the outstanding Office Action and in an informal teleconference between the Examiner and applicant's representative on August 2, 2005. The amendments are fully supported in the specification. Claims 6-8 and 13-16 have been withdrawn from consideration.

Rejection of claims 5 and 18, under 35 USC 112, second paragraph, with regard to the recitation of "**hybridizes specifically**"

The Examiner alleges that the recitation in these claims of a nucleic acid which "hybridizes specifically" to another nucleic acid is indefinite. Applicants disagree, for reasons that are of record. It is Applicants' position that the term would be well understood by one skilled in the art in light of the specification. For example, a skilled worker would recognize from what was known in the art at the time of filing the application and upon the reading the specification that a nucleic acid molecule which hybridizes specifically to a given nucleic acid is one that hybridizes preferentially to the given nucleic acid in comparison to a control and that is "long enough to hybridize effectively with the target sequence in a sample being probed." See, *e.g.*, the specification at page 10, lines 1-13, which further refers to typical specific primers or probes which contain the sequences of SEQ ID NO:7 (22 nucleotides), SEQ ID NO:8 (21 nucleotides), SEQ ID NO:10 (20 nucleotides) and SEQ ID NO:12 (26 nucleotides). Additional probes disclosed in the specification contain about 30 nucleotides. For example, the probe represented by SEQ ID NO:6 contains 29 nucleotides. Another probe that is about 20 nucleotides is represented by SEQ ID NO:5 (18 nucleotides). In spite of applicants' disagreement with the Examiner about this rejection, in the interest of expediting prosecution, and in accordance with the suggestion of the Examiner in the informal teleconference on August 2, 2005, independent claim18 and claims dependent thereon have been amended to clarify that the fragments are of about 20 to about 30 nucleotides.

Applicants request that the rejection be withdrawn.

Rejection claims 11 and 32, under 35 USC 112, first paragraph (scope of enablement), with regard to the recitation of tissue "**originating**" from the prostate

The Examiner alleges that the recitation in these claims of a tissue "originating" from prostate is broader than the scope which is enabled by the specification, *e.g.* because the recitation allegedly reads on metastasized cells which, in the view of the Examiner, do not necessarily overexpress the PB39 gene. Applicants disagree with the Examiner's interpretation, for reasons of record. Nevertheless, in the interest of expediting prosecution, and in accordance with the suggestion of the Examiner in the informal teleconference on August 2, 2005, claims 11 and 32 have been amended to recite that the sample is "from prostate tissue."

Applicants request that the rejection be withdrawn.

Rejections under 35 USC 112, first paragraph (written description and enablement) of claims that recite a nucleic acid that "**comprises**" the sequence of SEQ ID NO:1 or that "comprises" a sequence which is completely complementary to SEQ ID NO:1 (*e.g.* independent claim 17) or a nucleic acid that "comprises" the coding sequences of SEQ ID NO:1 or the complete complement thereof (*e.g.* independent claim 27). Claims reciting methods of using such nucleic acids (*e.g.* independent claims 19 and 30) are also rejected on the same grounds.

The Examiner alleges that the claimed nucleic acids read on a broad range of nucleic acids, including "full-length genes" (which term apparently refers to genomic DNA), and that the claims thus allegedly lack written description and enablement. Applicants disagree.

The Examiner has failed to establish a *prima facie* case that these claims lack written description, for at least two reasons: (1) An inventive feature of the claimed nucleic acid - the full-length sequence of the cDNA represented by SEQ ID NO:1, or the coding sequences thereof - is distinguishable from the genomic DNA, at least because the genomic DNA contains introns which are not present in SEQ ID NO:1. Attached is a cartoon (obtained from the NCBI web site) showing that the genomic DNA of PB39 contains a number of introns. Therefore, contrary to the allegation by the Examiner, the claimed nucleic acid does not read on genomic sequences. (2) Sequences located at the 5'

or the 3' ends of the claimed nucleic acid, which are encompassed by the term "comprising," include well-known sequences, such as vector sequences into which the cDNA can be cloned. Any substantial variability within the genus encompassed by the claims arises due to addition of elements that are not part of the inventor's particular contribution. Taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO:1.

Applicants wish to draw to the Examiner's attention the PTO's Training Materials with regard to the Written Description Guidelines, particularly Example 8 therein, which is attached for the convenience of the Examiner. The analysis in this example indicates that claims to a nucleic acid *comprising* a full-length, novel and non-obvious cDNA meet the requirements of 35 USC 112, at least with regard to written description. The claim under analysis in Example 8 of the training materials is directed to a cDNA (referred to as SEQ ID NO:2) encoding a full open reading frame (ORF); this is comparable to instant fact scenario, in which the claims are directed to a cDNA (SEQ ID NO:1) encoding the protein, PB39. Like the cDNA in the Example, the cDNA of the instant claims does not read on genomic sequences, at least because the cDNA does not contain introns found in the genomic DNA. Furthermore, like the claim of Example 8, the instantly claimed full-length cDNA sequence is novel and non-obvious.

The Example in the PTO's training materials acknowledges that "One of skill in the art can readily envisage nucleic acid sequences which include SEQ ID NO:2 because e.g. SEQ ID NO:2 can be readily embedded in known vectors." A similar point is also brought up by the Examiner in the Office Action of September 9, 2005. The Example goes on to say that "Although there may be substantial variability among the species of DNAs encompassed within the scope of the claim because SEQ ID NO:2 may be combined with sequences known in the art, e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO:2). Weighing all factors including (1) that the full length ORF (SEQ ID NO:2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession

of the genus of DNAs that comprise SEQ ID NO:2. **Conclusion: The written description is satisfied.**" Therefore, applicants urge that there is also adequate written description for the instant claims.

Furthermore, the Examiner has failed to establish a *prima facie* case that the instant specification fails to *enable* the claims which recite a sequence "comprising" SEQ ID NO:1 or coding sequence thereof. Applicants have taught how to make and use nucleic acids containing the cDNA sequences. The Examiner has obfuscated the enablement issue by focusing on sequences that may be on either side of the inventive cDNA sequences. See the discussion above with regard to the PTO's Training Materials (Example 8), where the Examiner is instructed not to consider the sequences located on either end of the novel and non-obvious cDNA sequences.

Applicants request that the rejections over 35 USC 112, first paragraph be withdrawn.

Anticipation rejection of claims 17 and 27 over alleged **prior art**

The allegation by the Examiner that the 321 nucleotide sequence disclosed by Hudson and/or the random hexamers disclosed in the Boehringer Mannheim kit anticipate these claims is unwarranted.

Even if sequences encompassed by "comprising" language of these claims were to be present at one or both ends of a nucleic acid of the sequence of SEQ ID NO:1, the coding sequences therein, or their complements, neither reference discloses the claimed sequences. That is, neither reference discloses a nucleic acid containing the sequence represented by SEQ ID NO:1 or the coding sequences thereof.

Neither of the cited references discloses all of the material elements of the claims, and therefore neither reference anticipates them. *In re Marshall*, 198 CCPA 344 (Fed. Cir. 1978).

Therefore, applicants request that the rejection be withdrawn.

At the suggestion of the Examiner in the informal telephonic interview of August 2, 2005, claims 17, 18, 19, 27 and 30 have been amended to clarify that a sequence which

is "completely complementary" to a second sequence is complementary to the complete length of the second sequence. The amendments do not narrow the scope of the claims and do not add new matter.

Anticipation rejection of claim 18 over alleged **prior art**

The random hexamer primers of the Boehringer Mannheim Biochemicals catalog do not anticipate claim 18, or claims dependent thereon. The random primers of the reference, which contain only 6 nucleotides each, do not contain the about 20 to about 30 nucleotides recited in claim 18.

The reference does not disclose all of the material elements of the claims, and therefore does not anticipates them. *In re Marshall*, 198 CCPA 344 (Fed. Cir. 1978).

Therefore, applicants request that the rejection be withdrawn.

In view of the preceding arguments and amendments, it is believed that the application is in condition for allowance, which action is respectfully requested.

Should any additional fee be deemed due, please charge such fee to our Deposit Account No.22-026, referencing docket number 31978-202420 and advise us accordingly. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Date: **December 1, 2005**

Nancy J. Axelrod, Ph.D.
Registration No. 44,014
VENABLE LLP
575 7th Street, NW
Washington, D.C. 20004-1601
Direct telephone: (202) 344-8334
Telefax: (202) 344-8300

DOCS #703294

Caveat: *In situations where the specification indicates that the SEQ ID NO: is a full-length cDNA open reading frame and the claim* ***cannot*** *read on a gene, the claimed invention would meet the written description requirement.*

Example 8: <u>DNA fragment Encoding a Full Open Reading Frame (ORF)</u>

Specification: The specification discloses that a cDNA library was prepared from human kidney epithelial cells and 5000 members of this library were sequenced and open reading frames were identified. The specification discloses a Table that indicates that one member of the library having SEQ ID NO: 2 has a high level of homology to a DNA ligase. The specification teaches that this complete ORF (SEQ ID NO: 2) encodes SEQ ID NO: 3. An alignment of SEQ ID NO: 3 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO: 3 and the consensus sequence of the known DNA ligases that are presented in the specification reveals a similarity score of 95%. A search of the prior art confirms that SEQ ID NO: 2 has high homology to DNA ligase encoding nucleic acids and that the next highest level of homology is to alpha-actin. However, the latter homology is only 50%. Based on the sequence homologies, the specification asserts that SEQ ID NO: 2 encodes a ligase.

Claim 1: An isolated and purified nucleic acid comprising SEQ ID NO: 2.

Analysis:

A review of the full content of the specification indicates SEQ ID NO: 2 is essential to the operation and function of the claimed invention. The specification indicates that SEQ ID NO: 2 encodes a protein that would be expected to act as a DNA ligase.

A review of the language of the claim indicates that the claim is drawn to a genus, i.e., any nucleic acid that minimally contains SEQ ID NO: 2. The claim is drawn to a nucleic acid comprising a full open reading frame. The claimed nucleic acid does not read on a genomic sequence because full-length mammalian cDNAs would not be expected to contain introns or transcriptional regulatory elements such as promoters that are found in genomic DNA. The claim reads on the claimed ORF in any construct or with additional nucleic acid residues placed at either end of the ORF.

The search indicates that SEQ ID NO: 2 is a novel and unobvious sequence.

There is a single species explicitly disclosed (a molecule consisting of SEQ ID NO: 2 that is within the scope of the claimed genus).

There is actual reduction to practice of the disclosed species.

One of skill in the art can readily envisage nucleic acid sequences which include SEQ ID NO: 2 because e.g. SEQ ID NO: 2 can be readily embedded in known vectors. Although there may be substantial variability among the species of DNAs encompassed within the scope of the claim because SEQ ID NO: 2 may be combined with sequences known in the art,

e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO: 2).

Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.

Conclusion: The written description requirement is satisfied.

Example 9: Hybridization

Specification: The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

Claim:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1,